REMARKS

Claims 1-15, 22-29, 34-41, 43-45, and 47-54 are now pending. In order to advance the prosecution of this reissue application. the claims are amended and claims 16-21, 42 and 46 are cancelled, without prejudice to the prosecution of subject matter cancelled by amendment in further patent applications. Various claims are amended, and new claims 51-54 are added. Neither the amendments nor the new claims constitute new matter.

In particular, the claims are amended, and new claims are added, to focus on the specific antibodies disclosed in the application, namely monoclonal antibodies 31.1 and 33.28, and chimeric antibody Chi #1, and their functional equivalents, meaning antibodies that competitively inhibit the binding of the recited antibodies to their target antigen, as well as antibodies that are raised against and bind to the specific target antigen. These amendments and the new claims are not new matter and are supported by the specification, *inter alia*, as follows:

> In a preferred embodiment, the antibody is the mouse monoclonal antibody 33.28 or 31.1 or an antibody which binds specifically to the same colon carcinoma-associated epitope as that bound by 33.28 or 31.1. In another preferred embodiment, the antibody is a mouse/human chimeric antibody Chi #1 that binds specifically to the same colon carcinoma-associated epitope as that bound by 31.1. (the '657 patent, column 4 lines 7-14)

and

> The specifically exemplified mAbs 33.28 and 31.1, and the chimeric antibody Chi #1 may be used to facilitate the production of additional mAbs which bind the same or immunologically cross-reactive colon carcinoma-associated antigens. First, these antibodies may be conjugated to a chromatographic support, and used to immunopurify colon carcinoma-associated antigens. These purified antigens, in turn, may be used to stimulate an immune response in suitable animals. Secondly, spleen cells from the responsive animals may be fused to immortalizing cells, and the resulting hybridomas screened for secretion of antibodies which bind to the purified antigen and/or whose binding to colon carcinoma-associated antigen is competitively inhibited by antibody 33.28 or 31.1, or chimeric antibody Chi #1. (the '657 patent, column 21 lines 3-16)

Given access to antibodies 33.1, 33.28 and/or Chi #1, the person skilled in the art would have been able to prepare and identify antibodies that competitively inhibit the binding of the parent antibodies and that recognize the same antigen using standard laboratory techniques well known in the art at the time the application that matured into the patent now is reissue was originally filed.

In addition, the specification and claims have been amended to correct a second error, namely the provision that the colon carcinoma associated antigens are not associated with any other forms of cancer. The specification contains statements and presents data which indicates that this is not the case (see, for example, the specification at column 4 lines 33-35, Tables 1 and 8, and Examples XI and XII at columns 29-30).

Further, it has been noted that claims 22, 23 and 47 contain an error, in that they relate to immunoassays for detecting the presence of colon carcinoma associated antigen in a sample. Both of these claims now recite steps for exposing the sample to antibody and then "detecting the binding of the antibody to the purified colon carcinoma associated protein antigen," which is an obvious error, since the antigen in the sample is not purified. Claims 22 and 23 are amended to delete the word "purified."

A number of minor typographical errors have also been detected, such as the omission of a hyphen in carcinoma-associated (*e.g.*, claims 22, 23), an extraneous hyphen (claim 25), improper antecedence in claims 33, 36, 37 and 41, and the recitation of "kilodalton" rather than "kilodaltons" (claim 44). These inadvertent errors have been corrected, and the corrections do not constitute new matter.

The Reissue Declaration has been revised to account for all the above-noted errors as well as to address other issues noted by the Examiner. The revised Reissue Declaration has been executed, in separate copies of the same document, by inventor Dr. Arlen and Assignee. Attorneys for Applicants have not as yet been able to obtain inventor Dr. Tsang's signature, and so, to ensure compliance with the legal requirements, Applicants submitt a Reissue Declaration by Assignee.

The original patent will be surrendered once Applicants are notified of the allowability of the subject matter.

A number of rejections and objections have been raised against the specification, the claims, and the Reissue Declaration. For reasons set forth in detail below, and in view of the amendments made herein and the documents submitted herewith, these rejections and objections should be removed and the claims should be allowed to issue.

1. The Form Of The Amendments Is Corrected

The manner is which amendments have been made in this application has been corrected, so that, relative to the original patent, all subject matter added is indicated by underlining and all subject matter deleted is indicated by bracketing, and, as required by the Examiner, all amendments shown are relative to the '657 patent and *do not take into account* previous amendments. We were advised by the Patent Office to insert identifiers such as "amended" and "new." Only those claims amended are set forth above but, for the Examiner's convenience, a complete set of claims, with amendments incorporated (*that is, the nature of the amendments are not shown*), is attached hereto.

2. The Amendments To The Specification Are Corrected

The specification is objected to because the specification had been amended to delete the date that the deposits of the three cell lines representing PCA 31.1, PCA 33.28 and Chi#1 were made, and because a hyphen was missing from HB 12315. In the amendments made herein these errors have been corrected.

3. The Objections To The Claims Are Obviated

Claims 30, 33 and 37 are objected to because claim 30 is said to lack the second container referred to in claim 34, claims 33 and 37 contain the typographical error "conation", and claim 2 contains the typographical error "3328" instead of "33.28."

In the amendments presented herein, all the noted errors are corrected.

4. The Claims Are Not Indefinite

Claims 1-50 are rejected under 35 U.S.C. §112 as indefinite for recitation of the phrase "said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions."

This phrase has been deleted from the claims, so that the rejection for indefiniteness should be removed.

5. The Claims Are Enabled

Claims 2-6, 17-29, 34-35, 38-41, 43, 47 and 49-50 are rejected under 35 U.S.C. §112 for lack of enablement because, according to the Examiner, the specification does not provide evidence that the claimed biological materials are either known and readily available to the public or reproducible from the written description record.

With regard to the information regarding deposit of cell lines PCA 31.1 and PCA 33.28, the information submitted to date has not completely addressed the issues because the date of deposit had been deleted from the specification, the form relating to the deposit of PCA 33.28 contained a credit card number and therefore could not be included in the public record, and the statement submitted from Dr. Arlen did not use exactly the same terminology for the deposited cells, and was not in the form of a declaration. The Examiner also queried why PCA 33.28 was not assigned a new deposit number. In addition, it was noted that the claims were not amended to recite the new accession numbers.

Applicants assert that the claims are fully enabled, and have amended the specification and claims and provided additional documentation and a Declaration of Dr. Myron Arlen (Exhibit C) to address the Examiner's concerns.

First, the specification has been amended to recite the dates on which PCA 31.1 and PCA 33.28 were deposited, which are September 22, 2000 and August 26, 2003, respectively. As proof of the deposits, Applicants submit herewith copies of the *International Forms* (as Exhibits A and B, respectively) for both hybridomas which demonstrates that they were deposited under the terms of the Budapest Treaty and were

found to be viable. As a result of these redeposits, correct samples of hybridoma lines recited in the specification, PCA 31.1 and PCA 33.28, will be available to the public from the ATCC and maintained for at least 30 years from the date of deposit or five years after the most recent request for a sample, whichever is longer.

Applicants supply herewith a complete copy of the papers filed August 29, 2003, with the credit card information redacted, in order to complete the record.

The Declaration by Dr. Arlen now refers, with specificity, to hybridomas PCA 31.1 and PCA 33.28, so that it is clear that the hybridomas identified in his declaration are the same hybridomas that were deposited and referred to in the specification. In addition, this second submission is presented in proper declaration form.

Finally, the specification and claims have been amended to recite the new accession numbers for PCA 31.1 and PCA 33.28, which are PTA-2497 and PTA-5413, respectively. The accession number for PCA 33.28 was not amended previously because Applicants were first informed of the new accession number in a letter dated September 24, 2003, *after* Applicants' previous submission.

For all the foregoing reasons, the claims are fully enabled and the rejections under 35 U.S.C. §112 should be withdrawn.

6. The Claims Satisfy The Written Description Requirement

Claims 1, 7-16, 30-33, 42, 45, 46 and 48 are rejected under 35 U.S.C. §112, as containing subject matter which does not satisfy the written description requirement because the claims are not limited by structure or molecular weight.

The claims are amended to provide for monoclonal antibodies as produced by hybridomas PCA 31.1 and PCA 33.28, antibodies that competitively inhibit the binding of said monoclonal antibodies to their respective target antigens, and antibodies that are raised against these target antigens. The scope of the claims has been narrowed to focus on the deposited monoclonal antibodies and chimeric antibody and the target antigens defined by these monoclonal antibodies, so that the written description requirement is satisfied.

7. The Amended Claims Are Not Anticipated

Claims 1, 8-9 and 16 are rejected under 35 U.S.C. §102(b) as anticipated by Herlyn et al., 1979, Proc. Natl. Acad. Sci. U.S.A. 76:1138 ("Herlyn"), because, according to the Examiner, Herlyn teaches antibodies to antigens from colon cancer cells that are not present on normal cells which are, contends the Examiner, the same antibodies as those claimed.

Claims 1 and 8 are rejected under 35 U.S.C. §102(b) as anticipated by Hollinshead et al., 1985, Cancer 56:480-489 ("Hollinshead"), because, according to the Examiner, Hollinshead teaches a monoclonal antibody to a colon carcinoma antigen which induces an immune response and is not present on normal cells. The Examiner contends that Hollinshead discloses "hybridomas which secrete antibodies that are directed to the same antigen that the claimed antibodies bind."

Claim 1 is rejected under 35 U.S.C. §102(b) as anticipated by Price et al., 1985, IRCS Journal of Medical Science 13:366-367 ("Price"), because, according to the Examiner, Price teaches an antibody to a colon carcinoma antigen that is not present in normal tissues which the Examiner presumes is directed to the same antigen to which the presently claimed antibodies bind.

Claims 16-21 are rejected under 35 U.S.C. §102(e) as anticipated by Hopp et al., United States Patent No. 4,703,004 ("Hopp"), because Hopp teaches anti-IgG antibodies, and monoclonal antibodies 31.1, 33.28, and Chi#1 are of the IgG subtype.

Without addressing the merits of the above rejections, by amending the claims to be restricted to monoclonal antibodies 31.1 and 33.28, chimeric antibody Chi#1, and their functional equivalents, the claims are clearly rendered novel over any of Herlyn, Hollinshead, and Price. None of these references disclose or enable the specific antibodies now claimed. Therefore, it is requested that the rejections of the claims over Herlyn, Hollinshead and Price be removed.

As regards the rejection over Hopp, claims 16-21 are cancelled (without prejudice), so that the basis for this rejection is obviated, and it should be removed.

8. The Amended Claims Are Not Obvious

Claims 1, 7-23, 30-33, 36-37, 42, 44, 45 and 46-49 are rejected under 35 U.S.C. §103(a) as obvious over Hollinshead and further in view of Neuberger et al., WO 86/01533 ("Neuberger"), or alternatively over Herlyn and Price in view of Neuberger, where Neuberger adds the disclosure of chimeric antibodies and antibodies that can be labeled with toxins, radiolabels, dyes, etc..

Because the claims have been amended to apply to specific monoclonal antibodies and their functional equivalents, neither Hollinshead, Neuberger, or their combination, nor Herlyn, Price, Neuberger, or any combination thereof, would render the claims obvious, because, taken singly or in any combination these references would not create any reasonable expectation of success in producing the claimed invention. Therefore, the rejections should be removed.

9. The Revised Reissue Declaration Is Not Defective

In view of the amendments to the specification and claims, submission of a new Reissued Declaration is required. The Examiner has objected to the original declaration because (1) the inventors do not state that they have reviewed and understand the amendments; (2) the priority claim lacks the series numbers for listed applications; (3) the declaration recites "potentially inoperative" rather than the mandatory phrase, "partly or wholly inoperative," and (4) the error in the deposits has not yet been corrected in the claims. Claims 1-50 are rejected as based upon a defective reissue declaration.

Applicants submit herewith a revised Reissue Declaration which addresses each of the foregoing issues, so that the objection and the rejection of the claims should be removed. Of note, inventor Dr. Arlen and Assignee have executed the revised Reissue Declaration, but Attorneys for Applicants have not yet obtained the signature of inventor Tsang. A copy of a draft of this response and the revised Reissue Declaration was sent to what is believed to be his current home address, (with a self-addressed return Federal Express envelope), on October 29, 2004, but no response or signed document has yet been received.

In view of the lack of Dr. Tsang;'s signature, and to fully address the objections made by the Examiner, Applicants further provide a Reissue Declaration By Assignee which, because this reissue application does not enlarge the scope of the claims of the original patent, should satisfy the legal requirements.

10. The Claims Are Not Indefinite

Claims 1-48 are rejected under 35 U.S.C. §112 as being indefinite for the following specific reasons

A. Recitation of "Membrane Fractions".

First, claims 1, 30, 34 and 38 and their dependent claims are indefinite for reciting "membrane fractions."

The claims are amended to delete reference to "membrane fractions," so that the rejection should be removed.

B. Reciting "Monoclonal Antibody Against A Monoclonal Antibody"

Claims 16-21 and 46 are rejected as indefinite for reciting "a monoclonal antibody against the monoclonal antibody" because it is unclear as to whether this refers to an anti-idiotype antibody, an anti-IgG antibody, an Anti-Fc antibody, etc..

Claims 16-21 and 46 are cancelled without prejudice to advance prosecution of this application, so that the rejection is obviated and should be removed.

C. Reciting "Normal Colon Cancer Free Human Tissue"

Claims 1, 30, 34 and 38 and their dependent claims are rejected for reciting the phrase "normal colon cancer free human tissue."

This phrase has been deleted from these claims, so that the basis for the rejection is obviated and the rejection should be removed.

D. Second Antibody To Said Antigen. . ."

Claims 30-41 are rejected as indefinite for reciting "second antibody to said antigen or an active component thereof" "because it is not clear what an active component of an antigen is" and the Examiner is not sure whether the "active component" refers to the second antibody or to the antigen.

Applicants have amended the claims to delete the objected to phrase, so that the rejection should be removed.

E. Antecedence for Antigen

Claim 6 is rejected as indefinite for reciting "said colon carcinoma-associated antigen in claim 2" as lacking antecedent basis, because claim 2 refers to Ab epitope.

The amendments to the claims obviate the basis for this rejection, which should be removed.

F. Inconsistent Accession Number

Claims 4-5, 19-20, 23, 25, 27, 28 and 34-37 are rejected as indefinite for reciting "antibody 31.1 (ATCC HB-12314)" in claims 4, 23, 25, 28 and 34 because it is unclear if this antibody is the same as PCA 31.1 which is indicated in the specification to correspond to accession number PTA-2497. Similarly, claims 2, 22, 24, 29 38, and their dependent claims are rejected for reciting antibody "33.28 (ATCC HB-12315)" because the specification refers to antibody PCA 33.28.

In response, Applicants would note, first, that the specification refers to the monoclonal antibodies produced by hybridomas PCA 31.1 and PCA 33.28 simply as, respectively, "monoclonal antibody 31.1" and "monoclonal antibody 33.28" (see, for example, column 4 lines 3-14). The "PCA" prefix is used only with regard to the hybridomas that produce the antibodies. That said, however, care has been taken to ensure that the PCA prefix is used consistently when referring to the hybridomas redeposited. In addition, these rejections are addressed by amendments to the claims which insert the "PCA" prefix when referring to the hybridomas and which contain the correct accession numbers for the redeposited materials

11. The Claims Do Not Contain New Matter And Satisfy The Written Description Requirement

Claims 2-6, 17-29, and 34-41 are rejected under 35 U.S.C. §251, as being based on new matter, or, alternatively, under 35 U.S.C. §112 for failing to satisfy the written description requirement.

The Examiner notes that the claims refer to "antibody 31.1 (ATCC HB-12314)", whereas the specification is amended to refer to "PCA 31.1" having accession number PTA-2497, and that the claims refer to "antibody 33.28.1 (ATCC HB-12315)", whereas the specification is amended to refer to "PCA 33.28." The Examiner queries whether the antibodies referred to in the claims and the specification are the same.

As discussed above, Applicants assert that the "PCA" prefix is used in the specification exclusively to refer to the hybridomas which produce the antibodies, which contain the same numerical designation but lack the "PCA" prefix. The claims have been amended to recite this distinction with particularity, and to recite the correct accessions numbers assigned after PCA 31.1 and PCA 33.28 were redeposited. The newly deposited material, and its accession numbers, constitute corrections of the erroneously deposited material, satisfies the written description requirement and is not new matter. Therefore, the rejections should be removed.

12. The Claims Are Enabled

Claims 16-21 and 46 are rejected under 35 U.S.C. §112 as unenabled.

As claims 16-21 and 46 are cancelled without prejudice, the basis for this rejection is obviated and should be removed.

CONCLUSION

For all the foregoing reasons, the rejections should be removed and the claims should be allowed to issue.

Dated: Nov. 5, 2005

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CLAIM LISTING WITH AMENDMENTS INCORPORATED

1. A monoclonal antibody specific for a purified human colon carcinoma-associated protein antigen,which is murine monoclonal antibody 33.28 as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413.

2. An antibody which competitively inhibits binding of the antibody of claim 1 to the human colon carcinoma - associated protein antigen.

3. An antibody according to claim 2 wherein said colon carcinoma-associated antigen is a protein having a molecular weight of about 61.1 kilodaltons.

4. A monoclonal antibody specific for a purified human colon carcinoma-associated protein antigen, which is mouse monoclonal antibody 31.1, as produced by hybridoma PCA 31.1 , deposited with the American Type Culture Collection and assigned accession number PTA-2497.

5. An antibody which competitively inhibits binding of the antibody of claim 4 to the human colon carcinoma - associated protein antigen.

6. An antibody according to claim 5 wherein said colon carcinoma-associated antigen is a glycoprotein, the protein component having a molecular weight of about 72 kilodaltons.

7. An antibody according to claim 1, 2, 4 or 5 immobilized on a solid phase.

8. An antibody according to claim 1, 2, 4 or 5 which is detectably labeled.

9. An antibody according to claim 8 wherein said detectable label is a radiolabel.

10. An antibody according to claim 1, 2, 4 or 5 conjugated to a cytotoxic radionuclide.

11. An antibody according to claim 1, 2, 4 or 5 conjugated to a cytotoxic drug.

12. An antibody according to claim 1, 2, 4 or 5 conjugated to a cytotoxic protein.

13. A composition comprising an antibody according to claim 10 in combination with a pharmaceutically acceptable carrier.

14. A composition comprising an antibody according to claim 11 in combination with a pharmaceutically acceptable carrier.

15. A composition comprising an antibody according to claim 12 in combination with a pharmaceutically acceptable carrier.

22. An immunoassay for detecting a colon carcinoma-associated antigen which binds to mouse monoclonal antibody 33.28 as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413, in a sample comprising:
(a) contacting said sample with an effective binding amount of the antibody according to claim 1 or claim 2; and
(b) detecting said antigen by detecting the binding of the antibody to the colon carcinoma - associated protein antigen.

23. An immunoassay for detecting a colon carcinoma-associated antigen which binds to mouse monoclonal antibody 31.1, as produced by hybridoma PCA 31.1, deposited with the American Type Culture Collection and assigned accession number PTA-2497, in a sample comprising:
(a) contacting said sample with an effective binding amount of the antibody according to claim 4 or claim 5; and

(b) detecting said antigen by detecting the binding of the antibody to the colon carcinoma - associated protein antigen.

24. A method for diagnosing colon cancer in humans comprising:
(a) removing a histological specimen from a patient suspected of having a colon cancer;
(b) contacting the specimen with monoclonal antibody 33.28, as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413;
(c) staining the specimen with an immunohistochemical stain; and
(d) detecting the presence of the antigen-antibody complex by the stain.

25. A method for diagnosing colon cancer in humans comprising:
(a) removing a histological specimen from a patient suspected of having colon carcinoma;
(b) contacting the specimen with mouse monoclonal antibody 31.1, as produced by hybridoma PCA 31.1, deposited with the American Type Culture Collection and assigned accession number PTA-2497;
(c) staining the specimen with an immunohistochemical stain; and
(d) detecting the presence of the antigen-antibody complex.

26. A method according to claim 24 wherein the stain is an avidin-biotin immunoperoxidase stain.

27. A method according to claim 25 wherein the stain is an avidin-biotin immunoperoxidase stain.

28. A kit for the immunohistochemical detection of colon carcinoma comprising:
(a) mouse monoclonal antibody 31.1, as produced by hybridoma PCA 31.1, deposited with the American Type Culture Collection and assigned accession number PTA-2497;
(b) reagents for immunoperoxidase and secondary antibody;

(c) immunoperoxidase; and
(d) colorizing reagents.

29. A kit for the immunohistochemical detection of colon carcinoma comprising:
(a) mouse monoclonal antibody 33.28, as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413;
(b) reagents for immunoperoxidase and secondary antibody;
(c) immunoperoxidase; and
(d) colorizing reagents.

30. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, said kit comprising a first container adapted to contain an antibody according to claim 2 or 5, and a second container adapted to contain a second antibody to said antigen said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

31. A kit according to claim 30 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

32. A kit according to claim 30 wherein the reporter molecule is an enzyme.

33. A kit according to claim 32 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

34. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, said kit comprising a first container adapted to contain monoclonal antibody 31.1, as produced by hybridoma PCA 31.1, deposited with the American Type Culture Collection and assigned accession number PTA-2497, to said antigen and a second

container adapted to contain a second antibody to said antigen, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

35. A kit according to claim 34 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

36. A kit according to claim 34 wherein the reporter molecule is an enzyme.

37. A kit according to claim 36 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

38. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, said kit comprising a first container adapted to contain monoclonal antibody 33.28, as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413 to said antigen and a second container adapted to contain a second antibody to said antigen, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

39. A kit according to claim 38 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

40. A kit according to claim 38 wherein the reporter molecule is an enzyme.

41. A kit according to claim 40 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

43. A chimeric antibody which is a chimeric mouse/human antibody Chi #1 as produced by the cell line deposited with the American Type Culture Collection and assigned accession number CRL-12316.

44. The chimeric antibody according to claim 43 wherein said colon carcinoma-associated antigen is a protein having a molecular weight of 72 kilodaltons.

45. A composition comprising the chimeric antibody according to claim 43 in combination with a pharmaceutically acceptable carrier.

47. An immunoassay for detecting a colon carcinoma-associated antigen which binds to the mouse/human chimeric antibody Chi #1 as produced by the cell line deposited with the American Type Culture Collection and assigned accession number CRL-12316 in a sample comprising:
(a) contacting said sample with the Chi #1 antibody; and
(b) detecting said antigen by detecting the binding of said antibody to the colon carcinoma - associated protein antigen.

48. A method for diagnosing colon cancer in humans comprising:
(a) removing a histological specimen from a patient suspected of having a colon carcinoma;
(b) contacting the specimen with a chimeric antibody according to claim 43;
(c) staining the specimen with an immunohistochemical stain; and
(d) detecting the presence of the antigen-antibody complex by the stain.

49. A method for diagnosing colon cancer in humans comprising:
(a) removing a histological specimen from a patient suspected of having a colon carcinoma;
(b) contacting the specimen with mouse/human chimeric antibody which binds to an antigen which binds to mouse/human chimeric antibody Chi #1 as produced by the cell

line deposited with the American Type Culture Collection and assigned accession number CRL-12316;

(c) staining the specimen with an immunohistochemical stain; and

(d) detecting the presence of the antigen-antibody complex by the stain.

50. A kit for the immunohistochemical detection of colon carcinoma comprising:

(a) mouse/human chimeric antibody Chi #1 (ATCC CRL-12316);

(b) reagents for immunoperoxidase and secondary antibody;

immunoperoxidase; and

(d) colorizing reagents.

51. An antibody which is raised against a purified human colon carcinoma associated antigen that is specifically bound by monoclonal antibody 31.1 , as produced by hybridoma PCA 31.1, deposited with the American Type Culture Collection and assigned accession number PTA-2497.

52. The antibody of claim 51 which is a monoclonal antibody.

53. An antibody which is raised against a purified human colon carcinoma associated antigen that is specifically bound by monoclonal antibody 33.28, as produced by hybridoma PCA 33.28, deposited with the American Type Culture Collection and assigned accession number PTA-5413.

54. The antibody of claim 53 which is a monoclonal antibody.

ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

International BioImmune Systems
Attn: Andrew Lin
225 W. Community Drive, Suite 140
Great Neck, NY 11021

Deposited on Behalf of: International BioImmune Systems

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse hybridoma cell line: PCA 31.1-AT	PTA-2497

The deposit was accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposit was received September 22, 2000 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested October 9, 2000. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Tanya Nunnally, Patent Specialist, Patent Depository

Date: February 6, 2001

cc: Lisa B. Kole

ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

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AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

International BioImmune Systems
Attn: Andrew Lin
225 W. Community Drive, Suite 140
Great Neck, NY 11021

Deposited on Behalf of: International BioImmune Systems

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse hybridoma cell line: PCA 31.1-AT	PTA-2497

The deposit was accompanied by: __ a scientific description _ a proposed taxonomic description indicated above.

The deposit was received September 22, 2000 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

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International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Tanya Nunnally, Patent Specialist, Patent Depository

Date: February 6, 2001

cc: Lisa B. Kole

ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

International BioImmune Systems, Inc.
Attn: Dr. Jeffrey I. Fasick
225 West Community Drive, Suite 140
Great Neck, NY 11021

Deposited on Behalf of: International BioImmune Systems, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse Hybridoma: PCA 33.28	PTA-5413

The deposit was accompanied by: __ a scientific description _ a proposed taxonomic description indicated above.

The deposit was received August 26, 2003 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested September 4, 2003. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris

Marie Harris, Patent Specialist, ATCC Patent Depository

Date: September 24, 2003

cc: Carmella L. Stephens
Ref: Docket or Case No.: A33081 072771.0106

AMERICAN TYPE CULTURE COLLECTION
10801 University Blvd.
Manassas, VA 20110-2209
Telephone: 703-365-2700
Fax: 703-365-2745

FACSIMILE

Date: September 4, 2003

To: Dr. Jeffrey I. Fasick
Fax Number: 516-773-8258

From: ATCC Patent Depository **Number of pages:** 1 (Including this page)

REFERENCE: Patent Deposit (Ref: Docket or Case No.: A33081 072771.0106)

Mouse Hybridoma: PCA 33.28 assigned PTA-5413.

Date of Deposit: August 26, 2003. Paperwork will be forwarded to you in a few days. An invoice will be sent under separate cover referencing your American Express account as follows:

Standard storage/informing	$ 1,150.00
Viability Test	320.00
Total amount to PTA-5413	$ 1,470.00

Marie Harris

Marie Harris, Patent Specialist
ATCC Patent Depository

ATCC

Patent Depository
10801 University Boulevard
Manassas, VA 20110-2209
Tel: (703) 365-2721
Fax: (703) 365-2745

FAX

To:	Dr. Jeffrey I. Fasick
Company	International BioImmune Systems Inc.
Fax No:	516-773-8258
# of Pages	2 (Including Cover Sheet)
From:	Marie Harris
E-mail:	mharris@atcc.org
Date:	September 19, 2003
Reference:	Lab copy of PCR Results - Patent Deposit PTA-5413 (PCA 33.28)

COMMENTS:

Attached is the lab copy of the results of PCR test on your material submitted for patent deposit purposes on August 26, 2003 for your information only.

Thank you

Marie Harris

Marie Harris

ATCC®
Mycoplasma Detection
PCR REPORT for

Customer Name: Farah Haq Order Number: in-house

	Customer Designation	ATCC Code	Amplified Product Detected[1]
A	NONE	Positive Control	yes
B	NONE	Negative Control	no
1	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]
3	PTA-5413	C4	no
4	[redacted]	[redacted]	[redacted]

1) This test is performed pursuant to licensing arrangements with Roche Molecular Systems, Inc. and Applied Biosystems. A positive report indicates detection of amplified DNA in the 200 – 400bp size range. A negative report indicates that there was no amplified DNA detected in the 200 – 400bp size range. Some samples are reported as needing further study to confirm initial results. Final results will be reported the following week.

DNA harvested from the above listed samples has been subjected to amplification by PCR using primers provided in the ATCC's Mycoplasma Detection Kit. These primers readily produce DNA fragments of characteristic size when the primers are allowed to amplify DNA from cultures containing *Mycoplasma arginini, M. fermentans, M. hominis, M. hyorhinis, M. orale, M. pirum, M. salivarium,* and *Acholeplasma laidlawii* as well as many other species of Mollicutes. While the primers exhibit excellent specificity, production of DNA amplicons in the 200-400bp size range from other prokaryotes such as certain strains of Lactobacillus, and Chlamydia has been observed. The primers may also amplify mycoplasma-specific DNA fragments from mycoplasma that have been inactivated by treatment with solvent, or other technique that leaves the mycoplasma DNA intact.

COMMENTS

Caliope Sarago	Biologist	9/12/03
Signature	Title	Date

Reviewed by: Debby Polayes

HP Officejet V Series V40xi
Personal Printer/Fax/Copier/Scanner

Log for
myron arlen md
5167738258
Sep 19 2003 2:48PM

Last Transaction

Date	Time	Type	Identification	Duration	Pages	Result
Sep 19	2:47PM	Received	703 365 2745	0:46	2	OK

In Re:	Tsang et al.		09/633,034
	(Applicant)		(Serial No.)
In Re:	Amendment*	August 26, 2003	A33081
	(Title of Paper)	(Date)	(File No.)

The stamp of the Patent Office Mail Room hereon acknowledges the receipt of the above-identified papers on the date indicated by such stamp.

* Fee Transmittal
Amendment Transmittal
Petition for Extension of Time
Verified Statement
ATTC Documentation (4 pages)

BAKER BOTTS LLP

Please type a plus sign (+) inside this box → ✚

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/633,034
Filing Date	August 4, 2000
First Named Inventor	Tsang et al.
Group Art Unit	1642
Examiner Name	Wells
Total Number of Pages in This Submission	
Attorney Docket Number	A33081-R

ENCLOSURES *(check all that apply)*

- ☑ Fee Transmittal Form
  - ☐ Fee Attached
- ☑ Amendment / Reply
  - ☐ After Final
  - ☑ Affidavits/declaration(s)
- ☑ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) *(please identify below)*:

Remarks ☐

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm *or* Individual name	BakerBotts LLP 30 Rockefeller Plaza New York, NY 10112
Signature	Carmella L. Stephens — Att Name: Carmella L. Stephens, PTO Reg: 41,328
Date	August 26, 2003

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on this date: August 26, 2003

Typed or printed name	Carmella L. Stephens		
Signature	Carmella L. Stephens	Date	August 26, 2003

BAKER BOTTS LLP

Attorney Docket Number: A33081-R

Title: MONOCLAONAL ANTIBODIES AGAINST HUMAN COLON CARCINOMA-ASSOCIATED ANTIGENS AND USES THERFOR

Use Space Below for Additional Information:

BAKER BOTTS LLP

FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 465

Complete If Known	
Application Number	09/633,034
Filing Date	August 4, 2000
First Named Inventor	Tsang et al.
Examiner Name	Wells
Art Unit	1642
Attorney Docket No.	A33081-R

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 02-4377

Deposit Account Name: Baker Botts LLP

The Commissioner is authorized to: *(check all that apply)*

☑ Charge fee(s) indicated below ☑ Credit any overpayments

☑ Charge any additional fee required under 37CFR 1.16 and 1.17

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20 =	0	X		=	0
Independent Claims		- 3 =	0	X		=	0
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	465
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 465

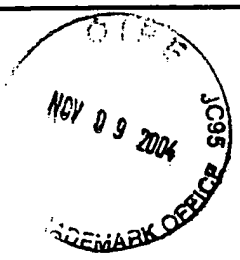
SUBMITTED BY

(Complete *if applicable*)

Name (Print/Type)	Carmella L. Stephens	*Registration No. (Attorney/Agent)*	41,328	*Telephone*	212 408-2539
Signature	Carmella L. Stephens			*Date*	August 26, 2003

BAKER BOTTS LLP

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) A33081-R



In re Application of	
Application Number 09/633,034	Filed August 4, 2000
For MONOCLAONAL ANTIBODIES * see attached	
Group Art Unit 1642	Examiner Wells

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

☐ One month (37 CFR 1.17(a)(1))	$_____
☐ Two months (37 CFR 1.17(a)(2))	$_____
☑ Three months (37 CFR 1.17(a)(3))	$ 930
☐ Four months (37 CFR 1.17(a)(4))	$_____
☐ Five months (37 CFR 1.17(a)(5))	$_____

☑ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ 465.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.

☑ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 02-4377. I have enclosed a duplicate copy of this sheet.

I am the ☐ applicant/inventor

☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☑ attorney or agent of record.

☐ attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a)_____.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

August 26, 2003
Date

PTO Reg No.: 41,328

Carmella L. Stephens
Signature

Carmella L. Stephens
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ Total of _____ forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Tsang et al.

Serial No.: 09/633,034 Examiner: Wells, M.

Filed : August 4, 2000 Group Art Unit: 1642

For : MONOCLONAL ANTIBODIES AGAINST HUMAN COLON CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR

AMENDMENT

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on:

August 26, 2003
Date of Deposit

Carmella L. Stephens — 41,328
Attorney Name — PTO Reg. No.

Carmella L. Stephens — August 26, 2003
Signature — Date of Signature

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed on February 26, 2003 received in connection with the above-identified application, Applicants provide the following amendments and remarks. Applicants also submit herewith a Petition to extend time for response for a period of three months from May 26, 2003 to August 26, 2003 accompanied by the appropriate fee.

IN THE SPECIFICATION:

Replace the paragraph starting at column 3, line 58 through column 4, line 2 with the following paragraph:

The present invention is also directed to a chimeric antibody specific for a human colon carcinoma-associated protein antigen wherein the antigen is not detectable on normal human tissues or on human carcinoma cells other than colon carcinoma cells. Mouse hybridoma PCA 31.1 has been deposited at ATCC and assigned [ATCC HB-12314] PTA-2497. Mouse hybridoma PCA 33.28 has been deposited at ATCC and assigned ATCC HB 12315. Cells transfected with chimeric 31.1 have been deposited at ATCC and assigned ATCC CRL-12316. The above deposits were made at American Type Culture Collection, at [12301 Parklawn Drive, Rockville, Md 20862 USA on March 13, 1997] 10801 University Boulevard, Manassas, VA 20110-2209.

IN THE CLAIMS:

1. (amended) A monoclonal antibody specific for a purified human colon carcinoma-associated protein antigen, wherein said antigen has the following characteristics:

(a) [said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions] said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity.

30. (amended) A compartmentalized kit for detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) [said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions] said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain an antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

33. (amended) A kit according to claim [30] 32 wherein the kit further comprises a third container adapted to conation a substrate for the enzyme.

34. (amended) A compartmentalized kit for detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) [said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions] said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain monoclonal antibody 31.1 (ATCC HB-12314) to said antigen and a second container adapted to contain a second antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

36. (amended) A kit according to claim [32] 34 wherein the reporter molecule is an enzyme.

37. (amended) A kit according to claim [33] 36 wherein the kit further comprises a third container adapted to conation a substrate for the enzyme.

38.(amended) A compartmentalized kit for detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) [said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions] said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain monoclonal antibody 33.28 (ATCC HB-12315) to said antigen and a second container adapted to contain a second antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

REMARKS

Claims 1-50 are pending in the application. For reasons detailed below, the rejections should be withdrawn and the claims allowed to issue. Entry of the foregoing amendments is respectfully requested.

1. The Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-50 are rejected under 35 U.S.C. §112, second paragraph. The Examiner alleges that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claims 1-50 are indefinite for reciting "said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions" in claims 1, 30, 34, and 38 because the exact meaning of the phrase is not clear. In addition claims 33, 36 and 37 recite "a substrate for the enzyme" and there is insufficient antecedent basis for this limitation in the claim.

In response to the rejections of the Examiner, Applicants have (i) amended subsection (a) of claims 1, 30, 34 and 38 to recite "said antigen is free of HLA-antigen and substantially free of non-immunogenic glycoproteins" and (ii) claims 33, 36 and 37 have been amended to correct the antecedent basis.

2. The Rejections Under 35 U.S.C. §112, First Paragraph

Claims 2-6, 17-29, 34-35, 38-41, 43, 47 and 49-50 are rejected under 35 U.S.C.§112, first paragraph. According to the Examiner, the specification does not

provide evidence that the claimed biological materials are (i) known and readily available to the public and (ii)reproducible from the written description.

Hybridoma cell lines 33.28, Chi#1, and 31.1 have been deposited with the American Type Culture Collection under the provisions of the Budapest Treaty. All restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application.

Additionally, as set forth in the attached Verified Statement of Dr. Myron Arlen, inventor of the above identified invention, the biological material described in the specification as filed is the same as that deposited in the ATTC. Furthermore, the deposited material was in Applicant's possession at the time the application was filed.

The Examiner alleges that the claims recite an antibody specific for a purified human colon carcinoma-associated protein antigen that is (i) characterized by a purification method; (ii) not detected in normal cells or in cells other than colon carcinoma; (iii) immunogenic; and (iv) induces an immune response. According to the Examiner, the specification only teaches a 61.1 kD and 72 kD protein with the claimed characteristics, however, the claims are broadly drawn to any molecular weight protein with the claimed characteristics. Thus, it would be reasonable to for one of skill in the art to conclude that the inventors were not in possession of the invention at the time the application was filed.

Applicants respectfully disagree with the Examiner. Applicants' pending claims encompass monoclonal antibodies that bind to an antigen with four different identifying characteristics, *i.e.*, (i) characterization by a purification method; (ii) absence in normal cells or in cells other than colon carcinoma; (iii) immunogenicity; and (iv) ability to

induce an immune response. In addition, as set forth in the specification, Applicants clearly demonstrated the production of monoclonal antibodies that bind to an antigen with each of these unique characteristics. Thus, one skilled in the art would conclude that the inventors were indeed in possession of the invention at the time the application was filed.

3. The Claims Are Not Anticipated

Claim 1, 8-9 are rejected under 35 U.S.C.§102(b) as being anticipated by Herlyn et al (PNAS 76:1138, 3/79;"Herlyn"). According to the Examiner, the claims recite an antibody specific for an antigen characterized by a purification and wherein the antigen is not detected on human carcinoma cells other than colon and is not detected on normal tissue and the antigen is immunogenic in human and induces an immune response and is radiolabeled.

The Examiner alleges that Herlyn teaches antibodies to antigens from colon carcinoma cells and the antibody does not bind to normal cells and the antibody is radiolabled. In addition, it would be inherent that the antigen would induce an immune response in humans because the antigen is not found in normal tissue. Thus the art reads on the claims.

Applicants assert that Herlyn fails to anticipate the claimed antibody molecules Herlyn's antibodies possess properties that differ from those of Applicants. One such property is the ability of Applicants' antibodies to stimulate an immune response in humans which is expressed as cell mediated immunity. Such immunity, referred to as antibody-dependent cellular cytotoxicity (ADCC) is associated with destruction of

tumors. Herlyn fails to disclose antibody molecules capable of such cell-mediated immunity. Further, Herlyn discloses that the 1083-17 and 1116-56 antibodies fail to bind to the colorectal carcinoma cell line SW480 (see, p.1439, column 2, first full paragraph). This is in contrast to Applicants' antibody molecules which clearly bind to SW480 cells (see, Table 4 of the specification).

Claims 1, 8 are rejected under 35 U.S.C.§102(b) as being anticipated by Hollinshead et al. (Cancer 56:480-489, 1985; "Hollinshead"). The Examiner maintains that Hollinshead teach monoclonal antibody to a colon carcinoma which induces an immune response and the antigen is not present in normal tissue and the antibody is used in an ELISA.

The claims are not anticipated by Hollinshead. First, Hollinshead merely discloses the purification of two colon carcinoma tumor associated antigens (TAA) and the use of those antigens in immunotherapy. Such immunotherapy involves the immunization of a subject with the purified TAAs for stimulation of a cell mediated immune response. Second, although Hollinstead ***mentions*** characterization of monoclonal antibodies against TAA, such characterizations are absent from the cited Hollinshead reference. Indeed, Hollinstead refers to the publication of such characterizations as "in preparation" (see reference 11 of Hollinstead).

Claim 1 is rejected under 35 U.S.C.§102(b) as being anticipated by Price et al (IRCS Journal of Medical Science 13:366-367, 1985;"Price"). The Examiner alleges that Price teaches an antibody to a colon carcinoma antigen wherein the antigen is in colon carcinoma cells and not in normal colon cells.

Applicants maintain that Price describes the production of a monoclonal antibody that is immunospecific for the ***anti-carcinoembryonic antigen*** (CEA). In contrast, Applicants have generated monoclonal antibodies against proteins other than that of CEA. In this regard, the Examiner's attention is directed to column 21, lines 63-66, of the specification which indicates that the purified colon carcinoma antigens utilized by Applicants to generate the claimed monoclonal antibodies were ***"distinct from that of carcinoembryonic antigen."***

Thus, given the differences between the disclosures of Herlyn, Hollinshead and Price and the subject matter encompassed by the pending claims, the claims cannot be anticipated.

4. The Claimed Invention is Not Obvious

Claim 1, 7-15, 30-33, 36-37, 42, 44, 45, 48 are rejected under 35 U.S.C.§103(a) as being unpatentable over Hollinshead as applied to claims 1 and 8 above, and further in view of Neuberger et al (WO 86/01533, published 3/86;"Neuberger").

The Examiner maintains that although Hollinshead does not teach a chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody, these deficiencies are made up for in the teaching of Neuberger. Neuberger is alleged to teach chimeric antibodies and antibodies that can be labeled with toxins, radiolables, dyes, cytotoxic agents and that the antibody can be immobilized for affinity chromatography. Therefore, according to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art at the time the

claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Hollinshead and Neuberger.

Claims 1, 7-15, 30-33, 36-37, 42, 45, and 48 are rejected under 35 U.S.C.§103(a) as being unpatentable over Herlyn or Price and further in view of Neuberger.

The Examiner alleges that although Herlyn and Price do not teach chimeric antibody or an antibody labeled with a cytotoxin, radiolabel, a kit comprising an antibody and a second antibody and a substrate for the enzyme, or a method of diagnosing colon cancer with a chimeric antibody. These deficiencies are made up for in the teaching of Neuberger. Neuberger is alleged to teach chimeric antibodies and antibodies that can be labeled with toxins, rabiolables, dyes, cytotoxic agents and the antibody can be immobilized for affinity chromatography.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have labeled the antibody and produce a chimeric antibody in view of Herlyn or Price in view of Neuberger et al.

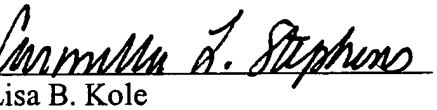
As indicated above, each of the Herlyn, Hollingshead or Price references fails to disclose monoclonal antibodies having the limitations set forth in the pending claims. The Neuberger reference fails to provide, or even suggest, the deficiencies found in the teachings of Herlyn, Hollingshead or Price. Thus, the claimed invention cannot be rendered obvious in view of the cited references.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by the amended claims is patentable over the rejections of the Examiner. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

Dated: August 26, 2003



Lisa B. Kole
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ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

International BioImmune Systems, Inc.
Attn: Dr. Jeffrey I. Fasick
225 West Community Drive, Suite 140
Great Neck, NY 11021

Deposited on Behalf of: International BioImmune Systems, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse Hybridoma: PCA 33.28	PTA-5413

The deposit was accompanied by: __ **a scientific description** __ **a proposed taxonomic description indicated above.**

The deposit was received August 26, 2003 **by this International Depository Authority and has been accepted.**

AT YOUR REQUEST: X **We** will **inform you of requests for the strain for 30 years.**

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested September 4, 2003. **On that date, the culture was viable.**

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris

Marie Harris, Patent Specialist, ATCC Patent Depository

Date: September 24, 2003

cc: Carmella L. Stephens
Ref: Docket or Case No.: A33081 072771.0106

BP4/9

ATCC®

BUDAPEST TREATY DEPOSIT FORM (BP/1)

American Type Culture Collection
P.O. Box 1549
Manassas, VA 20108

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF THE BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF A PATENT PROCEDURE

ALL QUESTIONS MUST BE COMPLETED IN ENGLISH. PLEASE USE ONE FORM FOR EACH STRAIN DEPOSITED.

1. Name of deposit. Please mark the appropriate box and provide the information requested for the material:

   - L **Microorganism** – the complete scientific name including genus and species plus the source of the material
   - L **Virus** – the name, whether plant or animal, and source including geographic location
   - X **Cell line** – the species and tissue of origin, geographical source of isolation, and any known associated hazards (HIV, EBV, etc.)
   - L **Genetic material** – the name of organism from which vector, clone or library is derived, the source of the DNA insert identified by species (e.g., human, mouse) or scientific name, the name of gene, and the identity of the host organism
   - L **Consortia or mixed culture** – the identity of each component of the mixture
   - L **Seeds, embryos, insect eggs, etc.** – the common name, the scientific name of the source of the deposit, and geographical source

   A mouse hybridoma cell line derived from fusion of SP2/0-Ag14 cells with spleen cells of Balb/c mice immunized with human colorectal carcinoma associated antigen

2. Strain designation* (i.e., number, symbols, etc). PcA 33.28
   ***The strain designation must correspond with the vial labels.**

3. Is this an original deposit under the Budapest Treaty? L Yes X No

4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty?
   X Yes L No
   If yes, please indicate ATCC designation. HB-12315

5. Is this deposit a mixture of microorganisms or cells? L Yes X No
   If yes, please describe:

6. Provide details necessary to cultivate, test for viability and store the deposit. If a mixture, provide description of components and a method to check for presence. If a plasmid, provide name of host and antibiotic resistance.
   Culture media: RPMI + 10% FBS + L-glutamine w/o Ca^{++} & Mg^{++}
   Viability test: Trypan Blue exclusion.
   Storage: -80°C ~~or liquid~~ in 90% FBS + 10% DMSO lowering 1°C/min then liquid N_2.

7. Provide sufficient description so that ATCC may confirm deposit properties (e.g., Gram negative rod).

   a. If deposit is a cell culture, is it being cultured in the presence of antibiotics? X Yes L No
      If yes, please list the antibiotics: Antimycotic/Antibiotic (Penicillin/streptomycin/amphotericin) from Gibco

   b. If deposit is a hybridoma, what is the isotype of the antibody produced? IgG1

8. Safety: Is this strain hazardous to humans? No Animals? No Plants? No

   If yes, what is the recommended biosafety level for working with this strain?
   (Refer to *Biosafety in Microbiological and Biomedical Laboratories*, 4th ed. HHS Publication No. (CDC) 93-8395. U.S. Department of Health and Human Services, Centers for Disease Control. Washington, DC: U.S. Government Printing Office; 1999. The entire text is available online at www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm.)

9. Regulatory Compliance:

   a. Was the material derived from a human? L Yes X No
   If yes, was an IRB-approved consent form (human subjects) obtained? L Yes L No

   b. Was this material obtained from wildlife? L Yes X No
   If yes, please indicate genus and species and whether wild or captive bred. _____

   c. Is work performed at your facility with exotic viruses affecting livestock and avian species? L Yes X No

   d. Identify any reagents of animal origin used to cultivate this organism/cell line (serum, growth factors, trypsin, etc.) and manufacturer, if known: FBS From Invitrogen/GIBCO

10. Availability:

Prior to issuance of a U.S. Patent, ATCC will only make a culture available as instructed by the depositor or relevant patent office. Samples must be provided to a specific investigator if a pertinent Patent Office under the Budapest Treaty instructs ATCC to do so. The following questions **must** be answered:

   a. As of date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to anyone who requests a culture? If yes, there are no restrictions on distribution. **Answering no will ensure the deposit is not available until the patent has issued.** L Yes X No

   b. As of the date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to requesters that satisfy Patent Offices in countries not signatory to the Budapest Treaty? L Yes X No
   If "yes," please state which countries: _____

   Please note that if you are converting your deposit to meet the requirements of the Budapest Treaty, and your deposit has already been released for distribution due to the issuance of a U.S. Patent, you **cannot** restrict it from further distribution. After a U.S. Patent issues and we are so notified, ATCC makes the culture available to anyone who requests it, as allowed under U.S. Patent and Trademark Office (USPTO) Rules and Regulations (37 CFR 1.808 [a][2]).

11. Notification: ATCC will notify you of your ATCC number after viability of the deposit has been confirmed.

Name of individual to notify: Dr. Jeffry I. Fasick
Fax: 516-773-8258 Phone: 516-773-8255 E-mail: Fasick_ibs@yahoo.com.

12. Payment by check or credit card (MasterCard, VISA or American Express) must accompany the deposit unless prior arrangements for billing have been made and approved. ATCC accepts purchase orders for the exact amount.

Purchase Order No. _____ Check No. _____
Credit Card number: [redacted] X MasterCard VISA American Express
Exp. Date: [redacted] Name shown on card: [redacted]
(Please print clearly or type)
Signature of card holder [redacted]

PAYMENT: ATCC MUST HAVE A BILLING ADDRESS, CONTACT PERSON, PHONE AND FAX FOR ALL DEPOSITS:

Contact Name: Dr. Jeffry I. Fasick
Billing Address: International BioImmune Systems, Inc.
225 West Community Drive, Suite 140 Great Neck, NY 11021
Phone: (516) 773-8255 Fax: (516) 773-8258

Do you have a current ATCC account number? L Yes L No

If Yes: ATCC Account Number = _____

If No: To apply for an account with ATCC, please complete a New Account Application located on our Web site (www.atcc.org) and return it with supporting documentation to ATCC for approval.

13. Name, address, phone and fax number of your Attorney of Record.

Carmella L. Stephens of Baker Botts LLP.
30 Rockefeller Plaza NewYork, NY 10112 phone: 212-408-2500
Fax: 212-408-2501 (Ref: Docket or Case No. A33081 072771,0106)

14. **MUST BE COMPLETED.** Deposited on behalf of: (Verify with your management who owns the deposit. The owner is usually a company or institution, and not an individual.)

International BioImmune Systems, Inc.

I understand and agree that the deposit may not be withdrawn by me for the period specified in Rule 9.1 of the Budapest Treaty (at least 30 years after the date of deposit or 5 years after the date of the most recent request for the deposit, whichever is longer), and that if a culture should die or be destroyed during the life of the patent, or the period of time so specified, it is my responsibility to replace it with a living culture of the same organism or cell. In the cases of viruses, cell cultures, plasmids, embryos, and seeds, it is my responsibility to supply a sufficient quantity for distribution for the period of time specified above.

Jeffry I. Fasick Jeffry I. Fasick 8/22/03
Printed Name Signature Date

Address. 225 West Community Drive, Suite 140 Great Neck, NY 11021

Phone: (516) 773-8255 Fax: (516) 773-8258 E-mail: fasick_ibs@yahoo.com

SHIPPING INFORMATION

BEFORE SHIPPING, PLEASE CONTACT THE ATCC PATENT DEPOSITORY FOR SHIPMENT ADVICE:

Fax: (703) 365-2745
E-mail: PatentDeposit@atcc.org

SHIPPING NOTICE:

The depositor is ultimately responsible for the shipment of deposits to ATCC and compliance with all applicable government regulations for the packaging and movement of the material. The depositor shall indemnify ATCC, to the extent permitted by law, against claims resulting from the violation of applicable government regulations caused by the depositor's shipment of deposits to ATCC.

STORAGE & FEES

Storage: Cultures are stored for 30 years from date of deposit or five years after the last request for a sample, whichever is longer, as required under the rules of patent offices in most countries.

Fees: All fees are subject to change. For current fees and other information, check our Web site at www.atcc.org or request a quotation of fees by e-mail at PatentDeposit@atcc.org or fax: (703) 365-2745.

ATCC USE ONLY: ATCC DESIGNATION_____ REC'D _____ V.T. RESULT_____

ATCC

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

International BioImmune Systems
Attn: Andrew Lin
225 W. Community Drive, Suite 140
Great Neck, NY 11021

Deposited on Behalf of: International BioImmune Systems

Identification Reference by Depositor:	**Patent Deposit Designation**
Mouse hybridoma cell line: PCA 31.1-AT	PTA-2497

The deposit was accompanied by: __ a scientific description _ a proposed taxonomic description indicated above.

The deposit was received September 22, 2000 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested October 9, 2000. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Date: February 6, 2001

Tanya Nunnally, Patent Specialist, Patent Depository

cc: Lisa B. Kole

A33081 072771.0106

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Tsang	
Serial No.	:	09/633,034	Examiner: Wells, M.
Filed	:	August 4, 2000	Group Art Unit: 1642
For	:	"MONOCLONAL ANTIBODIES AGAINST HUMAN COLON CARCINOMA-ASSOCIATED ANTIGENS AND USES THEREFOR"	

VERIFIED STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231
Sir:

The following hybridoma cell lines were redeposited with the American Type Culture Collection (ATTC) after the effective filing date of the above identified patent application:

31.1- (deposited September 22, 2000; PTA-2497); and
33.28- (to be deposited on August 25, 2003).

The biological material described in the specification as filed is the same as that deposited in the ATTC. Furthermore, the deposited material was in the Applicants' possession at the time the application was filed.

Respectfully submitted,

Date: 08/22/03

NY02:363011.1